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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,809	07/03/2001	Raghavan Rajagopalan	MRD/63	5120

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EXAMINER

TUCKER, ZACHARY C

ART UNIT	PAPER NUMBER
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1624

MAIL DATE	DELIVERY MODE
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05/07/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/898,809

Applicant(s)

RAJAGOPALAN ET AL.

Examiner

Zachary C. Tucker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-14 and 23-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-14 and 23-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 July 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>26Sep06</u> | 6) <input type="checkbox"/> Other: _____ |

Note Change of Examiner

This application is now before Zachary C. Tucker, primary examiner in Art Unit 1624. The prosecution history has been studied and the examiner understands the issues currently being debated.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 23 November 2005 has been entered. It requests that the amendment submitted after final rejection, under 37 C.F.R. 1.113, be entered. The amendment has been entered.

Declaration under 37 C.F.R. § 1.132

The declaration made by John K. Buolamwini, Ph.D., filed 23 November 2005 (hereinafter "Buolamwini Declaration") has been entered into the record and fully considered by the examiner.

Status of Claim Rejections - 35 USC § 112

In the previous Office action, claims 12-14 and 23-33 were finally rejected under 35 U.S.C. 112, first and second paragraphs, for reasons of said claims being 1. indefinite in scope, 2. not fully enabled by the disclosure, and 3. failing to comply with the written description requirement of the first paragraph of 35 U.S.C. 112.

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At issue is the functional language by which the radical "E" is described in instant claims 12 and 32 (the independent claims).

In the previous Office action, the examiner found that applicants' previous filing of a declaration under 37 C.F.R. 1.132, authored by Bernard F. Erlanger, was insufficient to overcome the rejections of record.

Presently, applicants have filed another declaration under 37 C.F.R. 1.132, authored by John K Boulamwini, which purports to address the issues raised by the examiner in the previous Office action. It is noted that Dr. Boulamwini is a full professor in the Department of Pharmaceutical Sciences at the University of Tennessee, and therefore would be expected to be conversant in the relevant arts (defined by the previous examiner in this case as "medicinal chemistry," particularly with respect to "small molecule ligands" [ligands of, presumably, receptors, enzymes and other types of protein molecules]).

Despite Dr. Boulamwini's high level of expertise, the declaration suffers from the same principal defect as does the previously filed declaration made by Dr. Erlanger, specifically that the author's description of what one of ordinary skill would consider to be within the scope of the instant claims, and how one of ordinary skill would go about determining it is not commensurate in scope with the claims' actual language. Very narrow examples are provided by the declarant as to what, for example, "carbohydrate receptor binding molecules," "steroid receptor binding molecules" and "somatostatin receptor binding molecules" would encompass (declaration, pages 4-6). If the claims actually recited only these *examples* provided by Dr. Boulamwini of each alternative recited in the definition of "E," the rejections at hand likely might not have been maintained. It is clear that applicants wish for "E" in the instant claims to embrace much more than only the

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examples provided by Dr. Buolamwini in the declaration at hand (and Erlanger, in the previously filed declaration).

There appears to be also a failure on the part of applicants to understand the exact basis for the findings of the instant claims' unpatentability . At issue is the lack of any specific structure/function relationship known by those of ordinary skill in the art which relates to the *full scope* of all of the alternative functionalities recited in the definition of "E," not a lack of known structure/function rules relating to the structure and function of the *sulfenate* group. Arguments framed in reference to a (perceived) rejection of the instant claims under 35 U.S.C. 112, based on a contention that there are no structure/function relationships known by practitioners of ordinary skill relating to the structure and function of sulfenate groups or moieties are, as was stated in the previous Office action, "not on point." The structure of the sulfenate group, which is part of the molecular structure of the compounds employed in the practice of the method according of the instant claims is known – it is explicitly set forth in the claims.

Page 7 of the declaration includes the statement that the declarant does not know more than about 10 high affinity selective receptor types for any particular ligand. To suggest that the instant claims would only be limited to what is known by Dr. Boulamwini would not be accurate. In fact that statement does not actually relate to the rejection at hand because what is at issue is the scope of/enablement of molecules which *bind* to the receptors, not the scope of /enablement of the receptors themselves. The *receptors* to which the moieties recited in "E" bind are understood with respect to their structure and and function much better than molecules which can bind to such receptors.

Molecules which bind to the specified receptors do not have structures which follow any particular rule. Dr. Boulamwini states that the medicinal chemist one can envision that there might already exist [sic] such molecules or they could be discovered. The examiner does not disagree with this statement, but the fact that the existence of molecular structures corresponding to the full scope of each alternative recited in the definition of variable "E" is *conjecture* is exactly one of the reasons that the rejections at hand have been set forth. A chemist of ordinary skill can understand the *function of* each alternative recited in the definition of "E," but the scope of which types of structure correspond to that function is only partially known. Dr. Boulamwini, as stated *supra*, provides as examples some of the most commonly known entities corresponding to each alternative recited in "E," but the claim is not limited in scope to only those which are commonly known.

The methodology by which Dr. Boulamwini proposes to practice the invention (declaration, pages 7-9) is not *per se* implausible, but the literature search he describes for determining molecules which bind to the chosen receptors would not and could not provide all of the necessary information for devising the *full scope* of the "E" group in the sulfonate compounds. This is because compounds which are *not* known in the literature are embraced by the instant claims. In other words, applicants, should the present claims be patented, would have the right to exclude others from practicing a method according to the instant claims, where "E" is some novel molecular structure which was neither conceived of by the applicants nor described in the literature. Such a method (where "E" is some structural entity neither conceived of by applicants nor described in the literature) would be

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an invention in its own right, yet would be embraced by applicants' claims. Should the present claims be patented, applicants could preempt the future work of others.

Another salient point raised in the previous Office action but which was not addressed in the present declaration, is the fact that carbohydrate receptors, as a class, is not well described and is poorly understood. The term "carbohydrate receptor" differs from the other types of "receptors" specified in the definition of "E" in that carbohydrates are neither a hormone nor a neurotransmitter (it is noted that "heat sensitive bacterioendotoxin" is neither a hormone nor a neurotransmitter as well, but this term is quite narrow when compared with the scope of all "carbohydrates"). So, any compound, which can bind to any enzyme, from any organism, is embraced by the term "carbohydrate receptor binding molecules." Of course, enzymes which bind to carbohydrates are not the only possible type of carbohydrate receptors, carbohydrate binding molecules come from a hugely more diverse group than do steroid receptors, neurotensin receptors, bombesin receptors, cholecystekinin receptors and somatostatin receptors.

Also, the term "carbohydrate receptor binding molecules" is indefinite in scope because what exactly is to be considered a "carbohydrate," in the context of the instant claims, is not clear and well-defined when the term is read in light of the instant specification. In the present declaration, Dr. Boulamwini states that the glycoprotein hormone receptor is an example of a molecule to which carbohydrates will bind. A chemist of ordinary skill would consider a glycoprotein to be a type of *protein* more so than a type of carbohydrate. The fact that glycoprotein hormone receptor is provided as an example of a carbohydrate receptor creates uncertainty about what other types of molecules, which normally would *not* be considered a "carbohydrate receptor" are indeed supposed to be

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carbohydrate receptors in the context of the instant claims. For example, are DNA and RNA binding enzymes “carbohydrate receptors?” DNA and RNA, as applicants can appreciate, have carbohydrate residues as part of their general structure.

In summary, the rejections at hand have not been overcome by the declaration authored by Dr. Boulamwini. This is principally because a literature search will not and cannot reveal all that is necessary for a skilled artisan to determine the full scope of, and make all of the alternatives recited in the definition of ‘E’ in the instant claims. Molecular structures which are not known are within the scope of the instant claims, because only the function is specified – any structure capable of performing the specified function would be embraced by the claim, but a chemist of ordinary skill cannot determine all such structures by performing a literature search. The declaration is not sufficient to overcome the rejections of record also because the fact that one of ordinary skill can identify *some* of what is within the scope of a claim (as is done in the declaration) does not show that the full scope of that claim is known.

To practice the claimed invention, one of ordinary skill would have to conduct a very large amount of experimentation. The examiner is aware that a requirement to conduct some experimentation is not fatal to a patent application’s enablement under 35 U.S.C. 112. Experimentation necessary for one of ordinary skill to practice the instant claimed invention, however, is undue because it would require the development of an indeterminate number of new molecular entities. This level of experimentation rises to the level of *invention*, as a matter of fact. It is not the type of experimentation which is necessary, for example, to develop pharmaceutical products from known compounds, or to

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devise a method of treating a disease with a known compound, given *in vitro* findings of that compound's pharmacological activity.

For reasons of record, and also for reasons explained in the preceding, claims 12-14 and 23-33 are rejected under the first and second paragraphs of 35 U.S.C. 112, for indefiniteness, lack of enablement, and failure to comply with the written description requirement.

The undersigned examiner has reviewed the prosecution history of the instant application, and agrees with the position taken by the examiner previously charged with its examination. Case law cited in the previous Office actions, mailed 9 February 2005 and 25 July 2005 is relevant to the issues at hand and provides legal authority for the Office's position.

The following is a new issue pertaining to the patentability of the instant application:

Specification

The specification is objected to under 37 C.F.R. 1.75(d), because the specification fails to provide proper antecedent basis for the claimed subject matter (see MPEP 608.01(o)). The original claims specify E to be selected from the group consisting of somatostatin receptor binding molecules, heat sensitive bacterioendotoxin receptor binding molecules, neurotensin receptor binding molecules, bombesin receptor binding molecules, cholecystekinin receptor binding molecules, steroid receptor binding molecules, and carbohydrate receptor binding molecules, and dihydroxyindolecarboxylic acid. However, the specification discloses E to be: somatostatin, heat sensitive bacterioendotoxin,

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neurotensin, bombesin, cholecystekinin, steroid, and carbohydrate receptor binding molecules, and dihydroxyindolecarboxylic acid. See page 7 and 8. Page 10 discloses E to be: either a hydrogen atom or selected from the group comprising antibodies, peptides, peptidomimetics, carbohydrates, glycomimetics, drugs, hormones, or nucleic acids. One can certainly see how all of the different receptor binding molecules could be used to target a compound to a particular cell or tissue, but the claims in their present form do not actually find antecedent basis in the specification.

Conclusion

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday to Friday from 9:00am to 5:00pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



ZACHARY C. TUCKER
PRIMARY EXAMINER